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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,844	01/09/2006	Ashwini Kumar Gupta	V0005.70100US00	1829
23628 7590 11/01/2007 WOLF GREENFIELD & SACKS, P.C. 600 ATLANTIC AVENUE BOSTON, MA 02210-2206			EXAMINER MABRY, JOHN	
			ART UNIT 4133	PAPER NUMBER
			MAIL DATE 11/01/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/527,844	Applicant(s) GUPTA ET AL.	
	Examiner John Mabry	Art Unit 4133	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 12 and 25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 12 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>none</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Examiner notes that there was no information disclosure statement filed with this application.

Objections

Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 12 is dependent upon claim 25. Dependent claims cannot precede the claim in which it is dependent upon.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 12 recites the limitation "a process as claimed in claim 25" in line one of claim 12. There is insufficient antecedent basis for this limitation in the claim.

The term "1r" in claim 2 is a relative term which renders the claim indefinite. The term "1r" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The Applicant does define the term "1r" anywhere in the claim. What does Applicant intend for "1r" to mean?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 12 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds and intermediates wherein R1, R2, R3 and R4=H and alkyl, does not reasonably provide enablement for R1, R2, R3 and R4=alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, alkylaryl, alkenylaryl, and alkynylaryl which includes heteroatoms in its carbon skeleton. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Pages 11-14 of the Specification describe starting materials and process for synthesis of compounds wherein R1, R2, R3 and R4=H and alkyl, but does not

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describe or list any reagents wherein compounds can be used to synthesize compounds wherein R1, R2, R3 and R4=alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, alkylaryl, alkenylaryl, and alkynylaryl which includes heteroatoms in its carbon skeleton.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims: Scope of the compounds. Owing to the range of many variables, millions of highly substituted 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole compounds are embraced.

(2) The nature of the invention: The invention is a highly substituted 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole compounds.

(3) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and chemical reactivity (which is affected by determinants such as substituent effects, bonding, molecular geometry, etc) is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(4) Direction or Guidance: That provided is very limited. Applicant shows a general synthesis of 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole of application's general formula 5a. Pages 11-24 of the Specification describes starting materials and process for synthesis of compounds wherein R1, R2, R3 and R4=H and alkyl, but does not describe or list any reagents wherein compounds can be used to synthesis compounds where R1, R2, R3 and R4=alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, alkylaryl, alkenylaryl, and alkynylaryl which includes heteroatoms in its carbon skeleton. There is limited evidence in the Specification of the example compounds that only covers no or a small portion of the substituents claimed of formula 5a. Thus, there is no specific direction or guidance regarding said compounds specifically mentioned in Scope.

The availability of the starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 2164.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or

apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court *in re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

(5) State of the Prior Art: These compounds are substituted 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole compounds wherein R1, R2, R3 and R4=H and alkyl, which are well documented in the art. So far as the examiner is aware, no substituted 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole compounds of general formula 5a wherein R1, R2, R3 and R4=alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, alkylaryl, alkenylaryl, and alkynylaryl which includes heteroatoms in its carbon skeleton. and wherein R3 and R4 being hydroxy or fluorine of any kind have been made or used.

(6) Working Examples: Applicant shows example 5a (page 13, line 14) but no working examples were shown wherein R1, R2, R3 and R4 equals aforementioned substituents have been made or used of any kind.

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(7) Skill of those in the art: The ordinary artisan is highly skilled, e.g. a masters or PhD level chemist.

(8) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has shown lack of enablement for the groups noted.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9, 12 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leguzza et al (EP 0207696 A1), in view of in view of Solomons et al (Organic Chemistry, 9th Edition, 2008).

The instant application claims a process for the preparation of a 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole (5a). The process begins with the reductive amination of a mono-protected cyclohexadione (1p) with NaCNBH₃ to form a protected 4-amino-cyclohexanone (2p) (a ketal). The protected 4-amino-cyclohexanone (2p) is deprotected to yield 4-amino-cyclohexanone (3a) which was subsequently treated with iodine and a substituted thiourea to yield the desired product, 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole (5a).

Scope & Content of Prior Art MPEP 2141.01

Leguzza et al discloses a process for the preparation of a 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole (5a). The process begins with the reductive amination of a protected cyclohexadione (1p) with NaCNBH_3 to form a protected 4-amino-cyclohexanone (2p) (a ketal). The protected 4-amino-cyclohexanone (2p) is deprotected to yield 4-amino-cyclohexanone (3a) and subsequently treated with bromine and hydrobromide to form an alpha bromoketone (not isolated). The alpha bromoketone was then reacted with a substituted thiourea to yield the desired product, 2-amino-4,5,6,7-tetrahydro-6-aminobenzothiazole (5a).

Differences between Prior Art & the Claims MPEP 2141.02

Leguzza differs from the instant invention in that Leguzza reacts protected 4-amino-cyclohexanone (2p) with bromine and hydrobromide to form the alpha bromoketone. Solomons discloses that it is beneficial to use iodine in place of bromide, because iodine is a better leaving group and it would result in a more facile substitution reaction (see pages 224-236, sections 6.2-6.9).

Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413

The Applicant is silent on the role of iodine in the final step to form desired product (5a); however the Examiner concludes that in Applicant's invention, the alpha

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iodoketone was form *in situ* and subsequent cyclization (substitution) occurred to form desired product (5a).

It would be obvious to one of ordinary skill in the art at the time that the invention was made to utilize iodine for bromine in the process of Leguzza since Solomons teaches that iodine is a better leaving group than bromine.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Pospisilik et al (WO 02/22590 A1) and Rao et al (GB 2394951 A) teach the process formula 5a. It is suggested that Applicant considers these references prior to responding to this Action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

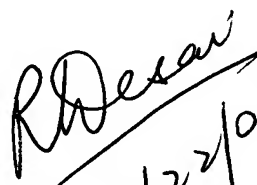
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry, PhD whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



JM


10/22/07
RITA DESAI
PRIMARY EXAMINER